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EXAMINER	
ROMEO, DAVID S	
ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/899,059	YU ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,29 and 35* is/are pending in the application.

4a) Of the above claim(s) *8-10,29 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-17,29 and 35* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1–17, 29 and 35 are pending.

Applicant's elected with traverse of group I, claims 1–17 and 29 in the reply filed on 06/14/2007. The requirement was deemed proper and was therefore made FINAL.

Claim 35 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 06/14/2007.

Applicant's elected the "inflammatory bowel disease" (IBD) species in the reply filed on 06/14/2007. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election was treated as an election without traverse (MPEP § 818.03(a)).

Claims 8–10 and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/14/2007.

In response to the Notice to the applicant regarding a non-compliant or non-responsive amendment (mailed 06/26/2008), Applicants' indicate (08/08/2008) that "colitis" (claim 11) reads on the elected species of "IBD." It is further noted that "colitis" (claim 11) is classed as an inflammatory bowel disease (IBD), not to be confused with irritable bowel syndrome (IBS). See the entry for "colitis" in Wikipedia. Therefore, claims 1–7 and 11–17 directed to the treatment of IBD, Crohn's disease or colitis are readable on the elected species "IBD."

Claims 1–7 and 11–17 are being examined to the extent that they are directed to or encompass the treatment of IBD, Crohn's disease or colitis. The other species listed in claims 1–

7 and 11–17 are independent or distinct because the divergent and non-overlapping pathologies involve distinct organs and/or tissues and are not so closely related that a search and examination of the entire claimed invention can be made without serious burden. The divergent and non-overlapping pathologies are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the pathologies would not render the claim obvious under 35 U.S.C. 103 with respect to the other pathologies. Clearly the species are not sufficiently few in number such that a search and examination of the entire claimed invention can be made without serious burden. The other species listed in claims 1–7 and 11–17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/14/2007.

Maintained formal matters, objections, and/or rejections:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 11, 12 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue that:

> As explained by the Federal Circuit, "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.;" Union Oil Co. of Cal. v. Atlantic Richfield Co., 208 F.3d 989, 997 (Fed. Cir. 2000). Here, one of skill in the art would readily understand what is encompassed by a protein with a sequence at least 95% identical to SEQ ID NO:20, and therefore antibodies that specifically bind and antagonize such proteins. Guidance is provided for making such proteins and antibodies throughout the specification, notably in paragraphs 256 and 298 as well as in Example 34. Therefore, the scope of the claimed invention is well supported in the specification, and Applicants respectfully request that the rejection be withdrawn.

Applicants' arguments have been fully considered but they are not persuasive.

The claims are directed to or encompass an antibody or fragment thereof that binds and antagonizes a "TNF-γ-β protein at least 95% identical to SEQ ID NO: 20." Thus, the claims are directed to or encompass an antibody or fragment thereof that binds and antagonizes a genus of TNF-γ-β proteins.

The specification provides a full-length TNF-γ-β polypeptide comprising the amino acid sequence of SEQ ID NO: 20 and several N-terminal deletions thereof ([0165]-[0166]). However, none of these constructs varies the amino acid sequence of SEQ ID NO: 20, other than by deletion, and thus these constructs are not representative of the genus. The specification and claim do not indicate what distinguishing attributes are shared by the members of the genus. The specification does not provide guidance regarding which variants within the genus have an activity that is antagonized by the antibody. Thus, the specification does not allow a person skilled in the art to visualize or recognize the identity of the members of the genus. In other words, the specification does not describe the subgenus of functional variants that have an activity that can be antagonized by the antibody in sufficient detail to allow a skilled artisan to

distinguish them from other variants within the genus of structural variants. No common structural attributes identify the members of the genus. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 20 and several N-terminal deletions thereof alone are insufficient to describe the genus.

The guidance at paragraphs [0256] and [0298] is general guidance, not specific guidance. The guidance in Example 34 only relates to SEQ ID NO: 20, not to the genus of variants. Furthermore, the court in University of Rochester v. G.D. Searle & Co., 358 F.3d 916 (Fed. Cir. 2004) held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of which peptides, polynucleotides, or small organic molecules have the desired characteristic the claims were not adequately described.

Just as in University of Rochester, the present application discloses a genus of chemical compounds (proteins having amino acid sequences at least 95% identical to SEQ ID NO: 20). Just as in University of Rochester, the present Specification does not guide the skilled artisan to the subset of proteins within the genus that are at least 95% identical to SEQ ID NO: 20 that have an activity that is antagonized by an antibody. The ability to screen for such variants does not make up for the deficiency of the Specification's description.

A genus must be described in some way that demonstrates to those of skill in the art that the applicant was in possession of the claimed genus at the time the application was filed. Applicants' have not shown that the recited genus was described in a manner that would show

possession of the genus to those skilled in the art. Without such a description, the claims lack an adequate written description.

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed method.

Claims 1–7 and 11–17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating IBD, Crohn's disease or colitis, does not reasonably provide enablement for a method of preventing IBD, Crohn's disease or colitis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants argue that:

> Applicants disagree with the Examiner's assertion that the results for TR6 shown in Zhang apply to the claimed invention, or that Zhang even shows a failure to prevent onset of an inflammatory disease. …the Examiner fails to explain what bearing the activity of TR6, a truncated receptor with different binding affinities, has on the present antibody-mediated methods. Zhang states that this incomplete inhibition by TR6 may very well be due to its binding of FasL and subsequent inhibition of FasL-induced apoptosis and activation-inducd T cell death. Zhang, page 1466, second column, second paragraph. Indeed, Figure 3 of Zhang shows a partial inhibition that is statistically significant compared to the controls. This inhibition combined with the significantly improved clinical outcome of Figure 6 actually supports the role of TR6 in both inhibiting and preventing the onset of disease.
>
> The Examiner conceded that the claimed methods are enabled for treating an inflammatory response. As preventing a disease affects the same interactions, a person of skill in the art would reasonably believe that the claimed methods would also prevent the same disorders. The Examiner provides no support that the complete abolition of a response is required for prevention. Citing evidence using

> different molecules that affect other pathways to support speculation that not only would the present antibodies have the same effect, but that partial inhibition equates with complete lack of prevention, does not undermine the reasonable expectation that the claimed methods would prevent as well as treat the listed diseases. …The enablement of a method of treating an inflammatory disease reasonably correlates with the method of preventing it, and the evidence cited by the Examiner does not rebut this.

The claims are directed to a method preventing IBD by antagonizing TNF-γ-β. In the last Office action the rejection stated that Zhang's TR6-Fc is a TNF-γ-β inhibitor. This is also recognized by the specification in Example 35. Therefore, the activity of TR6-Fc has a bearing on the present antibody-mediated methods.

It is acknowledged that "TR6 can bind to FasL and inhibit FasL-induced apoptosis in some experimental models" (Zhang (J Clin Invest. 2001 Jun;107(11):1459-68)), page 1466, right column, full paragraph 2). However, Zhang discloses that "These results as a whole suggest that the observed effects of TR6-Fc on the several in vitro and in vivo immune responses as examined in our study are not mediated via the Fas-FasL pathway due to their role in apoptosis induction" (page 1466, right column, full paragraph 2).

The argument that "a person of skill in the art would reasonably believe that the claimed methods would also prevent the same disorders" is unsupported by evidence and is, in fact, contravened by Zhang's results showing that TR6-Fc (a TNF-γ-β inhibitor) only inhibits, but does not prevent, in vivo and ex vivo splenic alloactivation in mice (Figure 3). Applicants' acknowledge that "Figure 3 of Zhang shows a partial inhibition." Although the results may have been "statistically significant," the inhibition with the TNF-γ-β inhibitor TR6-Fc was not complete even with high concentrations of the inhibitor (Zhang, page 1466, right column, full paragraph 1). Applicants' argument is mere argument.

Furthermore, "… in a chronic immune-driven inflammatory response there are a number of pathways that become engaged and can serve to sustain the inflammatory process" (Feldman (Transplant Proc. 1998 Dec;30(8):4126-7), page 4126, right column, last full paragraph), and "multiple costimulation pathways coexist" (Zhang, page 1466, right column, full paragraph 1). The claimed method relies on inhibiting a single pathway of stimulation. There are no working examples of "prevention." In view of these facts, it is reasonable to conclude that the claimed method of prevention is not enabled.

New Formal Matters, Objections and/or Rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

This application contains claims drawn to an invention nonelected with traverse in the reply filed on 06/14/2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, MANJUNATH RAO, CAN BE REACHED AT (571)272-0939.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE HTTP://PAIR-DIRECT.USPTO.GOV. CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

/DAVID S ROMEO/
PRIMARY EXAMINER, ART UNIT 1647

DSR
NOVEMBER 21, 2008